Calculating Hydration Entropy for Ionic Systems from Molecular Dynamics Trajectories

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Entropy calculation is a crucial topic in computational chemistry.[1] The Gibbs free energy governing the reactivity in chemical processes comprises of enthalpy and entropy. An accurate estimation method for entropy facilitates the computational investigation of chemical processes significantly. Hydration entropy is of special interest in drug design applications.[2] The association of a hydrated biomolecule and a hydrated small molecule leads to displacement of surface-bound waters into the bulk.[3] Therefore, calculating the affinity contributions from this displacement process is predicated on understanding the individual hydration entropy contributions in the non-associated state.

In our study we investigate monovalent cations as test systems to illustrate a novel approach to calculate hydration entropy from molecular dynamics simulation trajectories. Ions were chosen as a test set, as their spherical symmetry enables us to choose a convenient order parameter for the surrounding solvent molecules. We calculated the distribution of relative angular orientations of the dipole moment and the gradient of the electrostatic potential of the central ion within concentric shells around the ion. This allows us to represent the ordering influence of the ion within a scalar parameter. For validation we included Mg^{2+} into the test set due to the availability of consistent parameters. Results for the bivalent Mg^{2+} demonstrate that the approach extends to systems of a significantly different surface charge density. Other bivalent cations where omitted, as no parameters where available within the set of Aqvist et al.[4] included in the AMBER simulation package.

With the presented methodology we provide an approach to entropy calculation which does not require an assumption of harmonic potential energy surfaces. Furthermore, the density estimation procedure allows to generate a nonparametric estimate of state space probability density functions with limited sampling times. It should be noted, that the proposed procedure in it's presented form is only applicable to systems, wherein the ordering can be expressed within a one-dimensional parameter, which is the case for the spherically symmetric potential of the ions within this study. This limitation originates from the density estimation procedure used in this study. Using multidimensional density estimation, one can extend the approach to more complex systems.

References

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